ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Management of Nighttime Gastroesophageal Reflux Disease

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G&H What is the prevalence of nighttime GERD among GERD patients in the United States?

WO Approximately 14–20% of adults in the United States experience heartburn at least once a week, and among these individuals, approximately 70–75% experience heartburn at night at least once a week. These data come from results of two important epidemiologic studies by Farup and associates and Shaker and associates that found that between 70% and 75% of individuals with symptomatic gastroesophageal reflux disease (GERD) reported nighttime heartburn and that approximately 40% of these individuals reported that nighttime heartburn disrupted their sleep. The bottom line is that nighttime heartburn is very prevalent in GERD patients. Most GERD patients experience both daytime and nighttime symptoms, and it is relatively rare to encounter a patient who has only daytime or nighttime symptoms. I am not aware of any studies examining the prevalence of just nighttime GERD in the general population.

G&H Are the typical presenting symptoms of patients with nighttime GERD different from those of other GERD patients?

WO The most common GERD symptoms among individuals who have daytime and/or nighttime GERD are heartburn and regurgitation. Individuals who have significant nighttime GERD tend to have increased extraesophageal symptoms such as regurgitation compared to individuals with daytime GERD. Individuals with nighttime GERD may wake up more often choking or coughing or with regurgitation (ie, an acid or sour taste in their mouth) at nighttime. A recent study has also shown that individuals with nighttime heartburn tend to have more severe GERD symptoms.

G&H How does nighttime GERD heighten the risk of a more complicated disease course?

WO Individuals who have nighttime heartburn are certainly experiencing nighttime gastroesophageal reflux. In these individuals, episodes of nighttime reflux tend to have a longer acid clearance time, which means that they have a greater degree of acid mucosal contact for each reflux event. This is a problem because the length or duration of the acid mucosal contact facilitates the back diffusion of hydrogen ions into the esophageal mucosa, which causes esophageal injury. There are substantial data, consequently, to suggest that nighttime reflux is the primary cause of the complications of gastroesophageal reflux (ie, esophagitis) and respiratory complications such as chronic cough, wheezing, and exacerbation of bronchial asthma.

For some time, there has been a belief that reflux is just reflux, that it does not make a difference whether it occurs in the daytime or nighttime because it is still the same entity and it is still the same disease. However, there is increasing recognition amongst gastroenterologists concerning the importance of nighttime gastroesophageal reflux and the differences between the physiologic responses to acid mucosal contact during sleep and during the daytime. In that sense, nighttime GERD really constitutes a very different, much more serious entity.

G&H Have there been studies comparing different options for the treatment of nighttime GERD?

WO There have not really been any studies comparing proton pump inhibitor (PPI) treatments for nighttime GERD or for sleep disturbances associated with nighttime GERD. However, a clinical trial conducted by

Johnson and colleagues, which was published in the *American Journal of Gastroenterology*, did examine the use of 20 mg and 40 mg of esomeprazole (Nexium, AstraZeneca) versus placebo. The study showed that esomeprazole given once daily in the morning, as is normally prescribed, was very successful in relieving nighttime heartburn and sleep disturbance symptoms associated with nighttime heartburn.

G&H How does treatment for nighttime GERD differ from treatment for daytime GERD?

WO When meeting with a patient, I think that it is important to establish whether or not nighttime heartburn is an important component of the patient's symptom complex. If it is determined that the individual does have nighttime heartburn and consequently nighttime reflux, I would consider that individual as having a more "malignant" form of gastroesophageal reflux, and would treat him or her more aggressively, focusing on relief of nighttime reflux and nighttime symptoms.

Likewise, because nighttime GERD is a more aggressive form of the disease, a clinician may be more likely to perform an endoscopy on a patient in whom significant nighttime heartburn is suspected. Otherwise, as in a typical GERD case, endoscopy would not be normally involved if the patient is responsive to treatment.

G&H Do nighttime GERD patients require special follow-up?

WO In a patient with a suspected nighttime heartburn component, a clinician may choose to follow up with the patient more frequently to ensure that the nighttime symptoms are being relieved because, as previously mentioned, the continued presence of nighttime reflux is a significant factor in an individual who may be refractory to treatment. If the patient has any remaining residual nighttime symptoms, then it may be a good idea to perform 24-hour pH monitoring to more thoroughly assess the extent to which the treatment is resolving the nighttime reflux.

G&H Has there been any research investigating nonacid reflux events during sleep?

WO My colleagues at the Lynn Health Science Institute and I conducted a study to assess whether or not individuals who are taking twice-daily PPI therapy, which is currently fairly common in patients being treated for reflux, continued to have nighttime reflux (acid or nonacid) despite this powerful acid suppression. In addition, we wanted to investigate whether or not nonacid reflux was occurring at night and whether there was greater proximal migration of nonacid reflux, which might put the tracheal bronchial tree at risk. We found that giving individuals 40 mg of esomeprazole twice daily did reduce nighttime acid exposure, as expected. There was a continuation of nighttime reflux, and the majority of nighttime reflux events under those conditions were nonacid. We also found, however, that patients woke up as frequently or had arousal responses from sleep as frequently with nonacid reflux as with acid reflux, and there was no difference with the proximal migration of acid events versus nonacid events. This suggests to me that the esophagus is capable of recognizing nonacid reflux during sleep and providing the same protective measures that would be in place with nonacid events as with acid events.

G&H What research is currently ongoing in this field?

WO In nighttime reflux, there is a continuing interest particularly in individuals who may be considered "asymptomatic" but have "silent reflux." In other words, these individuals have reflux at night but have no obvious symptoms of heartburn. Because their nighttime reflux disturbs their sleep, the primary manifestation in many of these individuals is sleep complaint/disturbance. This is an area that my colleagues and I are currently researching further and preparing papers for publication. I think that this examination into the existence of gastroesophageal reflux in patients in whom it would never be expected will be a major area of future investigation.

Suggested Reading

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